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EXAMINER	
BETTON, TIMOTHY E	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,601	BUCAY-COUTO ET AL.	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-37* is/are pending in the application.

4a) Of the above claim(s) *22-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-21, and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed 5 November 2007 have been acknowledged and duly made of record.

The essence of applicants' arguments are drawn primarily to issue with the 112 rejection presented in the previous action. The matter of how the invention works is of importance in the scope of the current case due to certain limitations within the instant claims and how they may also be further interpreted based on such limitations. The art of ablation and the necrotizing of tissue are well-known. However, what is not so evident from the current invention are the elements which make this invention distinct in view of the common art of ablation. Furthermore, if the distinguishing factor of the invention is directed to particular dosage concentrations administered, the burden is on the applicant to further elucidate the central issue of the invention in view of these limitations.

However, in further reconsideration of the 112 rejection, the said rejection has been withdrawn.

Likewise, in reconsideration of the 103 rejection based on the amendment of instant claim 1, the said rejection is also withdrawn.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 17, and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Devane et al. (USPN 6,228,398 B1).

Devane et al. teach a multiparticulate modified release composition that in operation delivers an active ingredient in a pulsed or bimodal manner. The multiparticulate modified release composition comprises an immediate release component and a modified release component; the immediate release component comprising a first population of active ingredient containing particles and the modified release component composing a second population of active ingredient containing particles coated with a controlled release coating; wherein the combination of the immediate release and modified release components in operation deliver the active ingredient in a pulsed or a bimodal manner. The invention also relates to a solid oral dosage form containing such a multiparticulate modified release composition. The plasma profile achieved by the multiparticulate modified release composition is advantageous in reducing patient tolerance to the active ingredient and in increasing patient compliance by reducing dosage frequency (abstract only).

Devane et al. teach The present invention further provides a method of treating an animal, particularly a human in need of treatment utilizing the active ingredient, comprising administering a therapeutically effective amount of a composition or solid oral dosage form according to the invention to provide pulsed or bimodal administration of the active ingredient. Devane et al. teach any active ingredient for which it is useful to combine the advantages of a pulsatile plasma profile with a reduced frequency dosage regime may be used in practice of the present invention. Particularly useful in the practice of the invention include active ingredients whose pharmacological and/or therapeutic effects benefit from having a wash-out period

between plasma concentration peaks, such as those active ingredients susceptible to the development of patient tolerance[….] [C]hemotherapy agents such as vincristine, and analogues thereof column 6 lines 13-21 and lines 60-63.

Devane further teaches measurements in millimeters of dosage sizes for oral dosage forms.

IR components were formulated using three different sizes of non-pareil seeds having diameter dimensions of 0.5-0.6, 0.6-0.71 and 0.71-0.85 mm, respectively. The IR particles formed by coating 0.5-0.6, 0.6-0.71 and 0.71-0.85 mm nonpareil seeds were found to release 100% of the active ingredient within 20 minutes in aqueous media.

Devane et al. further teach an oral dosage from which is highly biodisintegrable (column 16).

Thus, Devane et al. adequately addresses the subject matter and the inventive objective of the claimed invention. Devane et al. anticipate instant claims 1-4, 6, 17, and 33-34 broadly. Particularly, Devane et al. teach chemotherapeutic agents which are none in art of cancer therapy as agents which cause ablation and necrosis of infected or tumorous tissue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-16, 18-21 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauschild et al., (USPN 6905475) and Escandon et al., (USPN 7015253) in view of Unger et al. (USPN 5469854) and Unger et al. (USPN 5733572).

Hauschild et al. teach a method and surgical instrument for treating prostate tissue including a surgical instrument having a main body, a needle deployment port, a needle, first and second handles and a lockout release mechanism to limit needle extension. Additionally, a kit includes the surgical instrument, together with a cystoscope, and optionally a syringe and reservoir of ethanol. The method includes needle-less injection and visualizing the ethanol injection by delivering both an echogenic agent and ethanol either by needle or needle-less injection or by providing an ultrasonically visible marker near the tip of the ethanol delivery cannula. The method also includes extending the needle transversely of the instrument housing using a link assembly (Abstract)."

In patented claim 1, Hauschild et al., teach a method of injecting a drug into prostate tissue. Column 3, line 30 specifically teaches the use of a surgical instrument: the scope allows visual positioning of the needle port against the urethra adjacent to the lobe of the prostate to be treated. The needle is advanced one detent click at a time to place the needle tip in the adenoma. A small volume of an active ingredient such as anhydrous alcohol is slowly injected into the tissue. The urethral lumen may be continuously irrigated while the ethanol is being administered. The embodiment suggests a process similar to a manner of necrotizing compromised tissue. However, in other aspects of the invention in Figures 9 and 10, column 6, lines 35-40, there is a disclosure of transurethral ablation. Furthermore, in column 1, line 39-57, ablation is initially

disclosed but in relation to laser treatments. Additionally, it is disclosed that ablation is associated with the process of surgically damaging prostate tissue. One of ordinary skill in the art would readily recognize that as a result of surgically damaging prostate tissue, there is certain to be necrotizing of said tissue. However, removal or excision of such compromised tissue is not as apparent. The dosage form of the active ingredient as disclosed in a specific embodiment is a sterile semi-solid in consistency, i.e., GELFOAM® Sterile Powder.

In column 10 of Hauschild et al., patented claim 1 is obvious over subject claim 8, which discloses an injection or insertion into the tissue via a jet injector. The referenced patent teaches a surgical instrument disclosed in column 5, lines 49 to 55 similar to the jet injector apparatus disclosed in instant claim 8. In addition, said instrument contains a disclosure as to make the needle more visible on ultrasound and ways to make the fluid delivered more visible which is similar to the disclosure of a contrast agent in instant claim 21.

Escanden et al. teach, "The present invention provides treatment regimens for treating diseased prostate tissue, including the steps of chemically ablating prostate tissue and coadministering an antiandrogen. In some embodiments, injection of ethanol, or an injectable gel comprising ethanol, into prostate tissue, chemically ablates prostate tissue. Steroidal and non-steroidal antiandrogens are suitable antiandrogens. One suitable non-steroidal antiandrogen is bicalutamide. The treatment regimen is suitable for treatment of prostate tissue diseases including benign prostatic hyperplasia and prostatic carcinoma. The invention further provides a treatment regimen for treating benign prostatic hyperplasia, including the steps of damaging prostate tissue and coadministering an antiandrogen. Also provided by the present invention is a kit for treating a human male, including a means for necrosing prostate tissue, an antiandrogen

drug, and a means for administering the antiandrogen drug. A kit including a first surgical device for delivering a chemoablation fluid to prostate tissue transurethrally, an antiandrogen drug such as bicalutamide, and a second surgical device for administering the antiandrogen drug, is further provided (Abstract)."

Specifically, Escanden et al. is obvious over instant claims 20 and 21 in instant application. In column 5 and 6 of referenced patent, several embodiments of chemoablation are cited. In one embodiment, the present invention provides a treatment regimen for treating diseased prostate tissue. The treatment regimen includes the steps of chemically ablating prostate tissue sufficiently to elicit a reparative process in the absence of further treatment; and coadministering a therapeutically effective amount of an antiandrogen.

"As used throughout this specification, the terms "ablate," "ablation" or "ablating" of tissue means causing a reduction in tissue mass. One suitable manner of ablating tissue is by causing a decrease in the number of tissue cells. The phrase "chemical ablation" includes processes whereby tissue mass is reduced by action of a chemical or biological agent on the tissue. The size of the prostate is reduced relative to its size prior to treatment by the treatment regimen. The treatment regimen is suitable for treatment of prostate tissue diseases including BPH and prostatic carcinoma. One suitable procedure for chemically ablating prostate tissue in accordance with the treatment regimen is by injection of ethanol (absolute alcohol) into the prostate to be treated. Ethanol preferably is injected deeply into prostate tissue through a needle that is positioned transurethrally, such as in the procedure known as transurethral ethanol ablation of the prostate (TEAP). The ablating action of ethanol is due to

several processes, including dehydration of cells, coagulation of proteins, and thrombosis of vessels that feed the tissue."

Column 17, the surgical instrument called a PROSTAJECT is similar in scope to the jet injector as disclosed in instant claim 8. Further, on line 11 the means for necrosing prostate tissue is disclosed. In particular, the ethanol is intended to be used as an ablating or necrosing agent, and the antiandrogen is intended to be coadministered according to any of the treatment regimens described above. The antiandrogens described above are suitable for the combination medicament. Bicalutamide in particular is a suitable non-steroidal antiandrogen (column 18). In column 10, line 11 an additive for enhancing the visibility of the chemoablation fluid may be incorporated via specialized dyes. This similarity is found like-wise in instant claim 21, which discloses imaging via contrast agents.

Hauschild et al. do not directly teach specific claims in regard to necrotizing prostate tissue, however a combination of a contrast agent (i.e., visible marker) and an ultrasonic beacon are disclosed within patented claims in order to facilitate detecting and determining amount of agent to specific site of prostate tissue via surgical instrument. Further, referenced patent does not teach an identical model of a jet injector as disclosed in instant claim 8, however the apparatus used is significantly similar in design, operation, and effect.

Escanden et al. does not teach the identical embodiment of contrasting agents as disclosed in instant application. Further Escanden et al does not teach treatment to other body regions except to prostate tissue.

However, The Examiner refers to Unger et al., which discloses, "Methods of and apparatus for preparing gas-filled liposomes are described. Gas-filled liposomes prepared by these methods are particularly useful, for example, in ultrasonic imaging applications and in therapeutic drug delivery systems." Where Hauschild et al and Escanden et al. are drawn to the actual use of a disclosed therapeutic delivery system, respectively, specifically for prostate tissue, Unger et al. encompasses all other embodiments disclosed within instant claims.

In column 4 under Brief Description of the Figures of referenced patent, adaptation of ablative formulation is adequately and comprehensively disclosed. As is lacking in subject claim 8 and the corresponding portion of the instant specification of the instant application, Unger et al. properly disclose what is obvious from Applicants' disclosure in claim 8. Additional adaptation disclosures are found in column 16, line 14-67, column 17, lines 1-18). Though Unger et al. patented invention is drawn to methods of and apparatus of preparing a formulation, the disclosure within column 4 teaches specific adaptation techniques in order to prepare an injectable or insertable dosage form for chemoablation. Unger et al. further teaches the functionality of the liposome dosage form with detailed explanations disclosed within column 11 to 15 of patented reference. It suggests the motivation to modify the matrical structure and pharmacodynamics (dosage form structure and shape and/or phase) of the liposome by making them single bilayer and/or multilamellar (column 11, line 52), viscosity modifiers (column 13, line 27), molecular weight polymers of 800 and 8000 (column 13, line 31, 32) for increased stability of dosage form structure, etc. Biodisintegrable disclosures of liposomes in their various modifications are also disclosed (column 14-18). As the motivation was obvious to present various dosage form shapes and biodisintegrable binders in subject claims 2-4 and 7-21,

respectively, so is the motivation obvious to combine the teachings of Hauschild and Escanden et al. with the specific dosage formulation disclosure of Unger et al. Furthermore, Unger et al. teach the expansive use of patented invention with a multiplicity of classes of drugs that can be formulated into said patented dosage forms (column 21-26). In particular, Unger et al. (USPN 5733572) teach the incorporation of ethanol for use in microsphere formulation. A skin absorption-enhancing agent may also be incorporated into the gas and gaseous precursor filled microspheres or into the aqueous media surrounding the gas and gaseous precursor filled microsphere structures. Such skin absorption enhancers include but are not limited to the following: alcohols such as ethanol, lauryl alcohol, linolenyl alcohol, 1-octanol, 1-propanol and 1-butanol; urea, cyclic unsaturated urea analogs, glycols, azone, n-alkanols, n-alkanes, orgelase, alphaderm cream and water. These may or may not be in a base which can be composed of various substances including but not limited to the following: glycerol, propylene glycol (PG); isopropyl myristate (1PM); urea in propylene glycol, ethanol and water; and polyethylene glycol (PEG). Unger et al., further still, includes a disclosure (column 32, Example 16, lines 14-24), which teaches a filtration process by which the resultant active ingredient (unfiltered volume) yield a volume of 80-90% of the unfiltered volume.

Claims 3,4, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauschild et al. (USPN 6905475) and Escandon et al. (USPN 7015253) as applied to claim 2-4 and 7-21 above, and further in view of Unger et al (USPN 5770222), Unger et al. (USPN 6443898), and Unger et al. (6123923).

Unger et al. (6443898) teach microspheres (bead, instant claim 3) that are disclosed to have a semi-solid consistency and are intended for use in a therapeutic drug delivery system [Detailed Description Text (87)].

Unger et al. (5770222) teach the final formation of gas-filled liposomes includ [ing] the transformation of the lipid to a solid form having a higher surface area, thus permitting better solubilization upon hydration and subsequently a higher yield of gas-filled liposomes [Detailed Description Text (101)].

Unger et al. (6123923) teach the incorporation of a glycolic acid polymer (film-forming material at the surface) so as to maintain stability of dosage form in association with solid matrices [Detailed Description Text (94)]. Further, Unger et al. teach fiber (instant claim 4) as a dosage form directed toward use as a contrast agent (instant claim 21) that is used in conjunction with ultrasound for surgical procedures [Drawing Description Text (10)].

Furthermore, instant claim 2 discloses a dosage form in the shape of a cylinder. The inner space of a needle (injection dosage form) cannula is shaped cylindrically, so as to accommodate various formulations that may be semi-solid within the needle housing, thereby properly addressing said limitation.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods and devices of Hauschild et al. and Escanden et al. to include administration of a chemical ablation agent/biodisintegrable formulation for insertion or injection in view of the motivation of Unger et al. as disclosed above. There is substantial documentation in the prior art, which suggests the motivation via obviousness to combine the teachings of Hauschild et al. and Escanden et al. by reasonable explanation of

producing an effective chemoablative/ therapeutic drug delivery system. It would instantly be obvious to one of ordinary skill in the art to see the motivation of Unger et al. in regard to disclosures/data supporting detailed explanations to purport the optimal scope of the subject invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shengjun Wang/
Primary Examiner, Art Unit 1617

TEB